## REMARKS

Claims 1-13 are currently pending in the application. Claim 4 is withdrawn. Claims 5, 8, and 9 are amended herein to make editorial changes to those claims. No new matter is added. Accordingly, upon entry of the amendment, claims 1-13 will remain pending in the application.

### *Claim Rejections – 35 U.S.C. §102*

Claims 1-3, 5-11, and 13 are rejected under 35 U.S.C. §102(b) as being unpatentable over U.S. Patent No. 5,891,432 to Hoo et al. ("Hoo"). Applicant respectfully disagrees and traverses the rejection.

In order to anticipate the invention, the cited reference must teach each and every element of the claim and the elements must be arranged as required by the claim (MPEP §2131). Despite the Office's assertions to the contrary, Hoo does not teach each and every element of the claims, and, therefore, does not anticipate Applicant's claimed invention.

The presently claimed invention is "a composition suitable for administration to a subject, said composition comprising an antigen bearing target and a fusion polypeptide, said fusion polypeptide comprising a first amino acid sequence which can bind to a carbohydrate and a second amino acid sequence comprising a ligand for a cell surface polypeptide of a leukocyte, wherein said composition includes said fusion polypeptide bound to a carbohydrate on said antigen bearing target and includes said polypeptide which is not bound to said antigen bearing target."

As an initial matter, Applicants respectfully point out that Hoo does not teach (1) a fusion polypeptide "comprising a first amino acid sequence which can bind a carbohydrate" and (2) that the "fusion polypeptide is bound to a carbohydrate on said antigen bearing target," as required by claim 1. Nor has the Office presented any evidence that Hoo teaches the feature of a fusion polypeptide which can bind a carbohydrate, or even this arrangement of the fusion polypeptide with the antigen bearing target.

Applicant asserts that Hoo instead teaches a transmembrane fusion protein (e.g., Example II of Hoo which teaches a membrane-bound GM-CSF/PDGFR fusion protein).

The Office Action at page 2 alleges that

> Contrary to Applicant's assertion, Hoo does teach a composition comprising fusion polypeptide that is bounded and not bounded to a cell. The Office directs Applicant's attention to Example II of Hoo. At the cited example, Hoo administered unwashed cells expressing the composition.

Applicant asserts that the Office has merely made conclusory statements regarding the presence of an unbound fusion polypeptide based on Hoo. The Examiner states at page 2 of the Office Action: "At the cited example, Hoo administered unwashed cells expressing the composition." The Examiner clearly has not articulated any reason that a fusion polypeptide having a transmembrane region could be released under the conditions recited in Hoo.

Applicant respectfully invites the Examiner's attention to Example II of Hoo at col. 25, lines 19-21, which plainly states:

> This example demonstrates that a cellular vaccine expressing a **membrane-bound** GM-CSF/PDGFR fusion protein can be used for tumor protection. [col. 25, lines 19-21; emphasis added]

Thus, it is not understood why the Examiner has taken a position that a fusion polypeptide having the transmembrane domain of the Platelet-derived growth factor receptor (PDGFR) expressed in a cell would be released from the plasma membrane in the absence of any further manipulation (e.g., washing). Because the cells of Hoo have been genetically engineered to express the fusion polypeptide, it would be apparent to one of ordinary skill in the art that the fusion polypeptide having a PDGFR transmembrane domain is inserted into the cellular membrane during synthesis of the protein.

Thus, the fusion polypeptide in Hoo referenced by the Examiner does not exist in bound and unbound fractions, regardless of whether the cells are unwashed. Nor does Hoo teach a composition comprising a fusion polypeptide which can exist in

bound and unbound fractions. Rather, Hoo teaches the attachment of a fusion protein to a cell by a variety of transmembrane domains (col. 7, ln. 21 – col. 8, ln. 14) that are inserted into the plasma membrane.

In contrast, Applicant's claimed invention provides a composition comprising "[a] fusion polypeptide comprising a first amino acid sequence which can bind to a carbohydrate." Because the fusion polypeptide of the invention is capable of binding a carbohydrate, it can exist in bound and unbound fractions with respect to the antigen bearing target. However, Hoo does not teach or suggest a composition containing a fusion polypeptide bound to a carbohydrate on the antigen bearing target. Accordingly, Hoo does not expressly anticipate the fusion polypeptide of the invention as claimed.

Nevertheless, the Office Action at page 2 states: "Thus, Hoo inherently teaches both bounded and unbounded compositions." However, MPEP §2112 (IV) directs that the Examiner must provide rationale or evidence tending to show inherency:

> "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993)…*In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). 'To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill'…*In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)…In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic **necessarily** flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). [emphasis added.]

The current law of the Doctrine of Inherency indicates that the claimed property must be the **necessary** consequence of the prior art disclosure. In other words, every time one conducts the prior art process, the claimed property **must** occur. If one conducts the prior art method and does not get the claimed property or therapeutic effect, then the claimed process is not inherent in the prior art.

However, there is nothing in Hoo that teaches or suggests any rationale that would necessarily result in an unbound fraction of a fusion polypeptide. This is

especially true given that the fusion polypeptides described by Hoo contain a transmembrane domain. Nor is there anything in the art at the time the invention was made that would address this deficiency of Hoo. Thus, Hoo does not teach an unbound fraction of a fusion polypeptide containing a transmembrane domain, even inherently. Regardless, Hoo does not teach a fusion polypeptide bound to a carbohydrate on an antigen bearing target, as required by the claims.

In view of the above, Hoo does not teach or suggest each and every element of the claims, currently presented. Because of this deficiency, Hoo cannot be used as the basis for a rejection under 35 U.S.C. 102(b). Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

***Claim Rejections – 35 U.S.C. §103***

Claims 1 and 12 are rejected under 35 U.S.C. §103(a) as being unpatentable over Hoo in view of Stray et al. (Glycobiology, 2000, 10(7): 649-658; "Stray") and Rott et al. (Med. Microbiol. Immunol., 1996, 184-193; "Rott"). Applicant respectfully disagrees and traverses the rejection.

In order to make out a *prima facie* showing of obviousness, the Examiner must establish that there is some motivation in one or the other of the cited references or in the state of the art at the time the invention was made to combine the references, the combination of references must teach or suggest each and every element of the claimed invention, and there must be some reasonable expectation of success in making and using the invention (MPEP §2143). In addition, "[a] patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art." *KSR International Co. v. Teleflex Inc*. 167 L. Ed. 2d 705, 712. Under section 103, "[b]oth the suggestion and the expectation of success must be founded in the prior art, not in applicant's disclosure" (*Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200, 1207, 18 USPQ2d 1016 (Fed. Cir. 1991), quoting *In re Dow Chemical Co.,* 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed Cir. 1988)).

Claims 1 and 12 presently recite "a composition suitable for administration to a subject, said composition comprising an antigen bearing target and a fusion

polypeptide, said fusion polypeptide comprising a first amino acid sequence which can bind to a carbohydrate and a second amino acid sequence comprising a ligand for a cell surface polypeptide of a leukocyte, wherein said composition includes said fusion polypeptide bound to a carbohydrate on said antigen bearing target and includes said polypeptide which is not bound to said antigen bearing target." As set forth above, Hoo does not teach or suggest any of (1) a fusion polypeptide "comprising a first amino acid sequence which can bind a carbohydrate;" (2) that the "fusion polypeptide is bound to a carbohydrate on said antigen bearing target;" and (3) that the composition includes a "[the fusion] polypeptide which is not bound to said antigen bearing target," as required by claim 1.

The Office has further cited Stray and Rott to remedy the deficiencies of Hoo. However, the Office's reliance on these references is misplaced. There is no motivation to combine Hoo with Stray and Rott to arrive at Applicant's claimed invention. Any such motivation is based on Applicant's disclosure and, therefore, is based on impermissible hindsight (MPEP §2145). Even assuming *arguendo* that there were a motivation to combine the references, the combination of references still does not properly place one in possession of a composition that includes a fusion polypeptide "bound to a carbohydrate on said antigen bearing target," and includes a fusion polypeptide "which is not bound to said antigen bearing target," as recited in the claims.

The Office Action at pages 6-7 alleges that it would have been *prima facie* obvious to combine the cited references: "In the instant case, at the time the invention was made, Hoo suggests the use of other membrane attachment domains and Stray et al. teaches that hemagglutinin, which has a membrane attachment domain that binds to sialic acid. Thus, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to use the membrane attachment domain of hemagglutinin as suitable alternative to the membrane attachment domain taught by Hoo." Applicant respectfully disagrees.

Stray teaches mechanisms of influenza virus infection, including mechanisms that involve hemagglutinin (Abstract). Rott teaches T-cell independent polyclonal B-cell activating properties of influenza A which are mediated by hemagglutinin (Abstract). Based on the teachings of Hoo, Stray, and Rott, one would not properly conclude that

the membrane attachment domain of hemagglutinin includes the sialic acid binding domain and/or binds sialic acid. As is apparent to one ordinarily skilled in the art, hemagglutinin has different domains and the sialic acid binding domain (HA1) of hemagglutinin is separate and distinct from its membrane-spanning region (HA2) (see e.g., specification at page 9, lines 13-15: "HA1 comprises significant sialic acid binding activity, while HA2 is anchored to the viral membrane and facilitates fusion of this membrane with a host cell membrane.").

Hoo specifically defines "membrane attachment domain" as "a domain that spans the width of a cell membrane, or any part thereof, and that functions to attach a polypeptide to a cell membrane." (col. 7, lines 10). Hoo also teaches that membrane attachment domains include "for example, the membrane-spanning region of an integral membrane protein such as a cell receptor or cell adhesion molecule." (col. 7, lines 2-27). Thus, based on Hoo, one would not view the entire cell receptor (e.g., hemaggluttinin) as a membrane attachment domain, as the Office has suggested. At best, one would only be motivated to use the membrane-spanning region of a cell receptor.

Even so, the Office has proposed that one would look to hemagglutinin because it is a cell receptor having a membrane attachment domain: "Stray et al. discloses that hemagglutinin has a membrane attachment domain, a cell surface binding moiety. The membrane attachment domain binds to sialic acid." However, Applicant asserts that the mere fact that hemagglutinin, which is a cell surface receptor, has both a membrane attachment domain and a sialic acid binding domain would not be sufficient to arrive at the claimed invention. Indeed, in *KSR International Co. v. Teleflex Inc.* (167 L. Ed. 2d 705, 712) the court stated: "[a] patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art."

Furthermore, neither Hoo nor Stray teaches or suggests why it would be desirable to include a carbohydrate binding domain in the fusion polypeptide of the invention. That is, in the absence of any guidance from Hoo or Stray, one would not have looked to include the hemagglutinin carbohydrate binding domain in a fusion polypeptide. Rather the motivation to include the hemagglutinin carbohydrate binding

domain in a fusion polypeptide is found in Applicant's disclosures, which teach that the fusion polypeptide is bound to an antigen bearing target by a carbohydrate binding domain. Notably, the fusion polypeptides exemplified in Applicant's specification were engineered not to include the HA2 domain of hemagglutinin (specification at page 181, lines 19-20), which anchors the protein to the viral membrane (specification at page 9, lines 13-15).

In sum, the Office has not made out a proper *prima facie* case of obviousness. The combination of cited references does not teach or suggest a composition that includes a fusion polypeptide "bound to a carbohydrate on said antigen bearing target" and a fusion polypeptide "not bound to said antigen bearing target," as required by claims 1 and 12. In further contrast to the cited references, the claimed invention does not require a membrane attachment domain that is a membrane-spanning domain (i.e., transmembrane domain). That is, even assuming *arguendo* that one would be motivated to combine the references, a fusion polypeptide as the Office has proposed would include the hemagglutinin molecule in its entirety in a fusion polypeptide. Because the fusion polypeptide proposed by the Office would include the hemagglutinin transmembrane domain, it would thus be bound to the antigen bearing target and, therefore, could not exist in an unbound form, as required by the claims. Additionally, the motivation cited by the Office to combine the cited references depends on the presence of a membrane-spanning domain as taught by Hoo. This feature of a membrane-spanning domain is nowhere recited in the instant claims. To arrive at such a rejection based on Hoo, Stray, and Rott appears based on impermissible hindsight reconstruction and, is therefore improper under 35 U.S.C. §103.

Thus, there is nothing in either of the cited references or in the state of the art at the time the invention was made that provides one of ordinary skill in the art with motivation to combine the references in the manner proffered by the Examiner. Assuming for the sake of argument that there were such motivation, the combination does not teach or suggest each and every element of the claimed invention. Therefore, because the cited combination of references does not put one of ordinary skill in the art

in possession of the claimed invention, one of ordinary skill in the art would not have a reasonable expectation of success in making and using the claimed invention.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1 and 12 under 35 U.S.C. §103(a)

## CONCLUSION

In view of the foregoing arguments, Applicant respectfully requests reconsideration and withdrawal of all pending objections/rejections and allowance of the application with claims 1-13 presented herein.

Applicants submit this paper in response to the Office Action dated February 5, 2010, in the above-referenced patent application with a request for 3-month extension of time, a Request for Continued Examination, and the requisite fees based on small entity status. Applicants believe that no additional fee is due to consider the present amendment. Nevertheless, the Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 85849DIV4(308597).

Dated: August 5, 2010

Respectfully submitted,

Electronic signature: /Elbert Chiang, Ph.D./
Elbert Chiang, Ph.D.
Registration No.: 60,325
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 517-5502
Attorneys/Agents For Applicant